SCIENTIFIC ABSTRACT OF THE TRIAL

Primary brain tumors in adults, principally the anaplastic astrocytoma and glioblastoma multiforme, are highly malignant and nearly always fatal. The primary objective of this Phase I study is to determine the toxicity of intratumoral injection of (H5.010CMV*hIFN-β*), a recombinant adenovirus expressing human interferon-beta in patients with recurrent or progressive anaplastic astrocytoma or glioblastoma multiforme.

We hypothesize that the direct injection of vector expressing hIFN-β will limit systemic exposure to the therapeutic agent and, therefore, minimize systemic toxicity. Local delivery of the vector to the tumor will achieve high concentrations of the therapeutic agent within the tumor. The toxicity and antitumor efficacy of H5.010CMV*hIFN-β* has not been previously studied in humans, although preliminary toxicology studies in rodents and non-human primates suggests that this approach can be safely undertaken. Preclinical testing in non-human primates indicates that systemic exposure to interferon-beta is low with toxicity confined to the local region of vector injection.

This study is open to patients ≥ 18 years of age with recurrent or progressive malignant glioma for whom surgical resection of the tumor is clinically indicated. Approximately 18 persons will be entered. Eligible individuals must be ambulatory and without other significant comorbidity. This is an open-label, inter-patient dose escalation (standard three-six–dose escalation) toxicity study. Each subject will receive two administration during the treatment phase of the study. The first administration will be given by stereotactic injection at ten sites within the tumor. The second dose will be administered one week later to ten sites at the margins of the remaining portion of the tumor immediately following surgical resection. Each study participant will remain hospitalized from the day before the first surgery until at least 4 days post-resection of the tumor and will be examined daily through Study Day 15. Patients will be seen in follow-up on Days 22 & 29, Months 2, 4, 6, 12, 18, & 24.

Our prior adenovirus based delivery of the herpes virus thymidine kinase gene (H5.010RSV-tk) using a similar adenoviral vector was generally well tolerated in patents with malignant gliomas using a similar clinical trial design (unpublished studies). This study will demonstrate the safety of this therapeutic approach, provide information on the most common adverse events and has the potential to demonstrate efficacy in patients with an otherwise incurable advanced malignancy.